

NCBI Entrez

## Protein QUERY

BLAST Entrez ?

Other Formats:

FASTA

Graphic

Links:

DNA

Related Sequences

LOCUS 1877288 200 aa  
 DEFINITION hypothetical protein Rv3557c. 17-JUN-1998  
 ACCESSION 1877288  
 PID g1877288  
 DBSOURCE - EMBL: locus MTCY6G11, accession Z92774  
 KEYWORDS  
 SOURCE  
 ORGANISM Mycobacterium tuberculosis  
 Bacteria; Firmicutes; Actinobacteria; Actinobacteridae;  
 Actinomycetales; Corynebacterineae; Mycobacteriaceae;  
 Mycobacterium.  
 REFERENCE 1 (residues 1 to 200)  
 AUTHORS Cole, S.T., Brosch, R., Parkhill, J., Garnier, T., Churcher, C.,  
 Harris, D., Gordon, S.V., Eiglmeier, K., Gas, S., Barry III, C.E.,  
 Tekai, F., Badcock, K., Basham, D., Brown, D., Chillingworth, T.,  
 Connor, R., Davies, R., Devlin, K., Feltwell, T., Gentles, S.,  
 Hamlin, N., Holroyd, S., Hornsby, T., Jagels, K., Krogh, A., McLean, J.,  
 Moule, S., Murphy, L., Oliver, S., Osborne, J., Quail, M.A.,  
 Rajandream, M.A., Rogers, J., Rutter, S., Seeger, K., Skelton, S.,  
 Squares, S., Squires, R., Sulston, J.E., Taylor, K., Whitehead, S. and  
 Barrell, B.G.  
 TITLE Deciphering the biology of Mycobacterium tuberculosis from the  
 complete genome sequence  
 JOURNAL Nature 393 (6685), 537-544 (1998)  
 MEDLINE 98295987  
 REMARK Erratum: [[published erratum appears in Nature 1998 Nov  
 12;396(6707):190]]  
 REFERENCE 2 (residues 1 to 200)  
 AUTHORS Parkhill, J.  
 TITLE Direct Submission  
 JOURNAL Submitted (11-JUN-1998) Submitted on behalf of the Mycobacterium  
 tuberculosis sequencing and mapping teams, Sanger Centre, Wellcome  
 Trust Genome Campus, Hinxton, Cambridge CB10 1SA Unite de Genetique  
 Moleculaire Bacterienne, Institut Pasteur, 28 rue du Docteur Roux,  
 75724 Paris Cedex 15, France E-mail: parkhill@sanger.ac.uk  
 COMMENT Notes:  
 Details of M. tuberculosis sequencing at the Sanger Centre are  
 available on the World Wide Web.  
 (URL, [http://www.sanger.ac.uk/Projects/M\\_tuberculosis/](http://www.sanger.ac.uk/Projects/M_tuberculosis/)) CDS have  
 been renumbered from the original cosmid submissions but the old  
 gene designations are in brackets after the new gene numbers.  
 Gene prediction was based on a Hidden Markov Model of TB genes  
 implemented in TBparse (Krogh) supplemented with visual inspection  
 of positional base preference in codons, especially where there is  
 an increase in the observed/expected third position G + C.  
 CAUTION: In some cases we may not have predicted the correct  
 initiation codon. Where possible we choose an initiation codon  
 (atg, gtg, or ttg) which is preceded by an upstream ribosome  
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 CDS 1..200  
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/note="Rv3557c, (MTCY06G11.04c), len: 200 aa. Probable transcriptional repressor, similar eg to Z95556|MTCY07A7\_12 Mycobacterium tuberculosis (215 aa) fasta scores, Opt: 215 z-score: 279.5 E(): 4.9e-08; 35.1% identity in 148 aa overlap; and YIXD\_BACSU P32398 hypothetical transcriptional regulatory protein (191 aa), fasta scores, opt: 169, E(): 4.2e-05, (23.9% identity in 188 aa overlap)"  
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the above report in   format

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Other Formats:

**FASTA****Graphic**

Links:

**DNA****Related Sequences**

LOCUS 2984362 192 aa 03-SEP-1998  
DEFINITION transcriptional regulator (TetR/AcrR family).  
ACCESSION 2984362  
PID g2984362  
DBSOURCE GENBANK: locus AE000776, accession AE000776  
KEYWORDS  
SOURCE Aquifex aeolicus.  
ORGANISM Aquifex aeolicus  
Eubacteria; Aquificales; Aquificaceae; Aquifex.  
REFERENCE 1 (residues 1 to 192)  
AUTHORS Deckert,G., Warren,P.V., Gaasterland,T., Young,W.G., Lenox,A.L.,  
Graham,D.E., Overbeek,R., Snead,M.A., Keller,M., Aujay,M.,  
Huber,R., Feldman,R.A., Short,J.M., Olson,G.J. and Swanson,R.V.  
TITLE The complete genome of the hyperthermophilic bacterium Aquifex  
aeolicus  
JOURNAL Nature 392, 353-358 (1998)  
REFERENCE 2 (residues 1 to 192)  
AUTHORS Deckert,G., Warren,P.V., Gaasterland,T., Young,W.G., Lenox,A.L.,  
Graham,D.E., Overbeek,R., Snead,M.A., Keller,M., Aujay,M.,  
Huber,R., Feldman,R.A., Short,J.M., Olson,G.J. and Swanson,R.V.  
TITLE Direct Submission  
JOURNAL Submitted (25-JUL-1997) Diversa Corporation, Genomics, San Diego,  
CA 92121  
COMMENT Method: conceptual translation.  
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181 elkkvlksai la  
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LOCUS 730078 210 aa 01-FEB-1995  
DEFINITION REGULATORY PROTEIN MTRR:  
ACCESSION 730078  
PID g730078  
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class: standard.  
created: Feb 1, 1995.  
sequence updated: Feb 1, 1995.  
annotation updated: Feb 1, 1995.  
xrefs: gi: 452332, gi: 438189, gi: 541020  
xrefs (non-sequence databases): PROSITE PS01081  
KEYWORDS TRANSCRIPTION REGULATION; DNA-BINDING; REPRESSOR.  
SOURCE Neisseria gonorrhoeae.  
ORGANISM Neisseria gonorrhoeae  
Eubacteria; Proteobacteria; beta subdivision; Neisseriaceae;  
Neisseria.  
REFERENCE 1 (residues 1 to 210)  
AUTHORS Pan, W. and Spratt, B.G.  
TITLE Regulation of the permeability of the gonococcal cell envelope by  
the mtr system  
JOURNAL Mol. Microbiol. 11 (4), 769-775 (1994)  
MEDLINE 94254732  
REMARK SEQUENCE FROM N.A.  
STRAIN=FA19  
COMMENT [FUNCTION] PUTATIVE REPRESSOR OF MTRC GENE. CONTROLS THE  
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[SIMILARITY] BELONGS TO THE TETR/ACRR FAMILY OF TRANSCRIPTIONAL  
REGULATORS.  
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BMJ 1998;316:166 (17 January)

## Editorials

# Is measles infection associated with Crohn's disease?

### *The current evidence does not prove a causal link*

The cause of Crohn's disease is likely to be multifactorial, and great interest was generated by two Swedish studies suggesting a high risk of Crohn's disease in those exposed to measles in utero.<sup>1 2</sup> The report in this week's issue from Nielsen et al (p 196),<sup>3</sup> however, is not alone in suggesting that there is no increased risk.

The two Swedish papers studied largely the same group of patients. Both studies were the result of two index cases of Crohn's disease noted to have been exposed to measles in utero (accounting for two out of four cases in the second study). The first report, in 1994, compared the expected and observed month of birth in patients with Crohn's disease born in 1945-54 in relation to the peak months of measles epidemics. The standardised incidence ratio was 1.46 (95% confidence interval 0.83 to 2.21) for future development of Crohn's disease for births during the three months after the peak incidence of measles. The second paper, in 1996, described a study of maternal measles infection in a cohort of 25 000 babies born in 1940-9.<sup>2</sup> Of four such cases three subsequently developed Crohn's disease.

In apparent support of the hypothesis, Thompson et al found a relative risk of 3.01 (1.45 to 6.23) for Crohn's disease among a British cohort of people vaccinated with live attenuated measles vaccine compared with a matched, unvaccinated group.<sup>4</sup> However, up to 74% of the original cohort were lost to follow up, and methods of follow up varied between the groups. This report led to concerns that vaccination with live, attenuated measles vaccine could confer the same risk as exposure to measles in utero.<sup>5</sup>

Now, however, four further studies have failed to confirm evidence of an association. Nielsen et al examined the health records of all possible cases of measles in pregnancy admitted to an infectious diseases hospital in the Copenhagen area in 1915-66.<sup>3</sup> The offspring of 25 women who had measles during pregnancy were identified, and none had developed Crohn's disease. In 1995 Hermon-Taylor et al compared the incidence of Crohn's disease with notifications of measles infection in England and Wales, including data after the introduction of measles vaccines.<sup>6</sup> They found no association. Also in 1997 Jones et al reported a case-control study of a large cohort of individuals exposed to viral infections during gestation, including 47 people exposed to measles in utero.<sup>7</sup> Follow up data on 88% found no cases of inflammatory bowel disease in the index cases, but two among the controls (one with Crohn's disease). A case-control study by Feeney et al in 1997 compared measles vaccination rates in 140 patients with inflammatory bowel disease (83 with Crohn's disease) and matched controls and found no association.<sup>8</sup>

To reconcile these discrepancies we need an understanding of the investigation of causation. Significant

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associations were established in the original studies, but associations may be artefactual, indirect, or causal. Artefactual associations may result from chance. The inclusion of index cases which have generated the hypothesis leads to reporting bias, especially if the numbers are small. Spurious associations may also result from differences in methods and completeness of data collection and recall bias (cases more often recall exposure to possible causal factors than controls). Some of these factors may have affected Thompson's vaccination study.<sup>4</sup> An indirect association is one in which the factor and disease are associated through a common third factor, such as malaria and altitude, linked through mosquitoes. There are no apparent indirect links in these studies.

A refinement of Koch's postulates has led to the development of six criteria to evaluate the likelihood that an association is causal, the first three of which are the most important.<sup>2</sup> Firstly, the greater the strength of the association (the higher the relative risk) the more likely it is that a factor is causal. A dose-response gradient and a consistent association—that is, one repeated in other studies—also suggest causality. The specificity of the association—whether the occurrence of the factor predicts the presence of the disease—the correct temporal association, and the biological plausibility of the association are also relevant. Only the last two criteria are met by the Swedish studies.

Thus, several recent studies of the association between measles and Crohn's disease have failed to confirm the original association, suggesting that the original finding was artefactual. The theory of measles as a causative factor in the development of Crohn's disease therefore cannot be upheld and should remind us of the need for rigorous methodological review when causal associations are proposed.

Jane Metcalf, *Senior registrar in gastroenterology*<sup>a</sup>

<sup>a</sup> Gloucestershire Royal Hospital, Gloucester GL1 3NN

1. Ekblom A, Wakefield AJ, Zack M, Adami HO. Perinatal measles infection and subsequent Crohn's disease. *Lancet* 1994;344:508-10. [Medline]
2. Ekblom A, Daszak P, Kraaz W, Wakefield AJ. Crohn's disease after in-utero measles virus exposure. *Lancet* 1996;348:515-7. [Medline]
3. Nielsen LLW, Nielsen NM, Melbye M, Sodermann M, Jacobsen M, Aaby P. Exposure to measles in utero and Crohn's disease: a Danish register study. *BMJ* 1998;316:196-7. [Full Text]
4. Thompson NP, Montgomery SM, Pounder RE, Wakefield AJ. Is measles vaccination a risk factor for inflammatory bowel disease? *Lancet* 1995;345:1071-4. [Medline]
5. Calman KC. Measles vaccination as a risk factor for inflammatory bowel disease. *Lancet* 1995;345:1362-4.
6. Hermon-Taylor J, Ford S, Sumar N, Millar D, Doran T, Tizard M. Measles virus and Crohn's disease. *Lancet* 1995;345:922-3.
7. Jones P, Fine P, Piracha S. Crohn's disease and measles. *Lancet* 1997;349:473.
8. Feeney M, Clegg A, Winwood P, Snook J. A case control study of measles vaccination and inflammatory bowel disease. *Lancet* 1997;350:764-6. [Medline]
9. Mausner JS, Kramer S, eds. *Mausner and Bahn epidemiology. An introductory text*. Philadelphia: WB Saunders Company, 1985.

## This article has been cited by other articles:

- Nicoll, A., Elliman, D., Ross, E. (1998). MMR vaccination and autism 1998. *BMJ* 316: 715-716  
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Elizabeth Miller, Pauline Waight, R G Pebody, M  
Paunio, P Ruutu, Ross Lawrenson, and Richard Farmer  
*BMJ* 1998 316: 1745. [\[Letter\]](#)

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Other Formats:

FASTA

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Links:

Related Sequences

LOCUS 481591 190 aa 20-FEB-1995  
DEFINITION hypothetical protein 4 - Clostridium pasteurianum.  
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PID g481591  
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PIR dates: 20-Feb-1995 #sequence\_revision 20-Feb-1995 #text\_change  
20-Feb-1995.

KEYWORDS .  
SOURCE Clostridium pasteurianum.  
ORGANISM Clostridium pasteurianum  
Eubacteria; Firmicutes; Low G+C gram-positive bacteria;  
Clostridiaceae; Clostridium.

REFERENCE 1 (residues 1 to 190)  
AUTHORS Meyer, J.  
TITLE Direct Submission  
JOURNAL Submitted (??-NOV-1993) to the EMBL Data Library

FEATURES Location/Qualifiers  
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121 nyvvhieefv kdameagsik kgnslfvaya flgtlcsvsl yevinaendn inntienlmn  
181 yilngiglqn  
//

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